Methemoglobinemia Following Monolinuron Ingestion
A Case Report in a Child

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Case: We describe a case report of a 2-year-old boy presenting to the emergency department with cyanosis and agitation. There was no suggestive history of poisoning but parents reported the presence of an aquarium at the family dinner the night before, with an aquarium cleaner beside it. Physical examination at admission revealed central cyanosis without signs of respiratory distress. Oxygen saturation measured by pulse oximetry (SpO2) was at 80% in room air. Plasma level of methemoglobin was measured at 11.8%. After 6 hours, methemoglobin decreased spontaneously to 5% and pulse oximetry saturation reached 98% in room air. Consciousness, weakness, and behavior were concomitantly improved. Because of rapid and spontaneous improvement, no specific treatment such as methylene blue was administered. A mass spectrometry toxicological analysis was performed in a blood sample taken the day of admission. Screening procedure of pesticides based on liquid chromatography coupled with mass spectrometry identified monolinuron, a phenylurea herbicide.

Conclusions: We recommend considering acquired methemoglobinemia after ingestion of industrial products and drugs in children with cyanosis, mental status alteration, and without respiratory distress symptoms.

Key Words: methemoglobinemia, monolinuron, ingestion

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described, and healthy patients usually exhibit very few symptoms limited to cyanosis when blood methemoglobin level is below 15%. Mental status alterations, headaches, tiredness, and syncope have been observed when methemoglobinemia reached level of 20% to 30% hemoglobinemia. Levels higher than 50% may cause seizures, coma, and death. Patients with comorbidities (anemia, cardiovascular disease, sepsis, or inherited disorders of hemoglobin) may experience symptoms at lower levels. In children, the risk of developing toxic methemoglobinemia is greater, which can be explained by the reduced cytochrome-b5 reductase activity in red blood cells. Indeed, Rechetzki et al. showed higher reference values in clinically healthy children (from 3.61% to 6.44%) than in adults (from 1.0% to 3.8%). Moreover, newborns are at increased risk of developing methemoglobinemia given that fetal hemoglobin is more sensitive to oxidation.

Methemoglobinemia may arise from various causes such as (1) congenital methemoglobinemia, with genetic factors leading to dysfunctional hemoglobin or enzymatic deficiencies; and (2) acquired methemoglobinemia, which is more common than the congenital form. This latter cause usually follows contamination by chemical products (nitrates/nitrites), industrial by-products (petrol octane booster, nitrobenzene, nitro-ethane-anilines, and copper sulfates), drugs (benzocaine, dapsone, metoclopramide, etc.), herbicides and pesticides though skin contact, inhalation, or ingestion. These agents can oxidize hemoglobin to methemoglobin through several mechanisms such as direct oxidation of hemoglobin (such as benzocaine, prilocaine), indirect oxidative pathways (such as nitrates), and via metabolic activation (such as aniline and dapsone).

Methemoglobinemia can cause a discrepancy between partial pressure arterial oxygen (PaO₂) and SpO₂ due to a leftward shift of the oxyhemoglobin dissociation curve. This explains the contrast between major cyanosis and normal measured PaO₂ of highest values when oxygen therapy is administered. In the current case, unfortunately, a venous blood gas analysis was performed as opposed to an arterial analysis. We thus recommend performing an arterial blood gas analysis in case of unexplained cyanosis.

When a child presenting with cyanosis and decreased of SpO₂ but without respiratory distress, physician should be attentive to others etiologies than commonly described: cardiovascular disease such as pulmonary arterial hypertension and congenital heart disease should be investigated at first with echocardiography when available; after that, arterial blood gases with a carboxyhemoglobin and methemoglobin measurements should be performed especially in children with history of intoxication.

First-line therapy for methemoglobinemia cases is to discontinue the offending agent. Methylene blue is an efficacious treatment and serves as a cofactor for the enzyme NADPH methemoglobin reductase. An administrated methylene blue dosing of 1 mg/kg contributes to reduce the ferric iron atom (Fe⁴⁺) back to the ferrous state (Fe²⁺) in the red blood cells and to decrease methemoglobin level. The other treatments to reduce methemoglobin level (blood transfusion, exchange transfusion, hemodialysis) have low success but some authors suggest that if methylene blue is unavailable, high-dose of vitamin C should be considered in patients without renal failure.

Monolinuron is an algaecide, which belongs to the chemical class of phenylurea herbicides, such as diuron, monuron, and others. Monolinuron is used to control broad-leaved weeds, blanket weed, and hair algae. Studies suggest that phenylurea algaecides bearing an O-CH₃ (methoxy) group on the nitrogen atom of urea can be metabolized to aniline derivatives. Then, aniline causes methemoglobinemia after oxidation via phenyl hydroxylamine, a metabolite.

Monolinuron poisoning has been rarely reported with only 2 published cases of intoxication by Gramonol (monolinuron/paraquat herbicide). Casey et al. reported the case of a 59-year-old man with a methemoglobinemia blood level at 52%, who subsequently developed multiple organ failure and died. Proudfoot described the case of a 63-year-old woman with methemoglobinemia at 36%, which was successfully treated with methylene blue and hemodialysis.

No data regarding monolinuron poisoning have been reported in children. According to the literature, neurological symptoms are described with higher methemoglobinemia blood level. In the current case, we assume that agitation may be due to the acquired nature of methemoglobinemia. We thus recommend investigating toxic causes of methemoglobinemia in patients with neurological symptoms associated with a methemoglobinemia blood level lower than 20%.

In conclusion, we recommend considering acquired methemoglobinemia after ingestion of industrial products and drugs in children with cyanosis, mental status alteration, and without respiratory distress symptoms.

REFERENCES